

2. RESPONSE/REMARKS

2.1 STATUS OF THE CLAIMS

Claims 1, 3-13 and 16-38 were pending at the time of the Action.

Claims 18 and 20-23 remain withdrawn as being directed to non-elected inventions.

Claims 1, 3-13 and 16-38 remain pending in the application.

2.2 THE REJECTION OF CLAIMS UNDER 35 U. S. C. § 103(A) IS OVERCOME.

The Action at pages 2-5 rejected claims 1, 3-13, 16-17, 19 and 24-38 under 35 U. S. C. § 103(a), allegedly as being unpatentable over Dekany et al., (Peptides 1996: Proc. 24th Eur. Peptide Symp.; Ramage and Ephron [Eds.], Mayflower Scientific, Kingswinford, England, 1998, pp 331-32; hereinafter "Dekany") in view of Neubert et al. (Pharm. Res., 6(9):743-749; hereinafter "Neubert").

Dekany is said to disclose "a lipidic moiety containing sugar compound" in which the lipidic moiety is attached to a monosaccharide *via* a linker. Dekany is said to "meet(s) the limitations of instant formula I for W being absent." (the Action at page 3, ¶ 3).

Neubert is said to teach that "the lipophilicity of drugs can be increased by ion pair formation with lipophilic counterions." (the Action at page 4, ¶ 2).

The Action also contends that it "would have been obvious to one of ordinary skill in the art....to make complexes of Formula I and their compositions as instantly claimed with a reasonable expectation of success, since the prior art teaches the preparation of such complexes using the components as instantly claimed." (the Action at page 4, ¶ 1).

In each of these conclusions, Applicants respectfully traverse.

A finding of obviousness under 35 U. S. C. § 103 requires a determination of the scope and content of the prior art, the level of ordinary skill in the art, the differences between the claimed subject matter and the prior art, and whether the differences are such that the subject

matter as a whole would have been obvious to one of ordinary skill in the art at the time the invention was made. *Graham v. John Deere Co.*, 148 USPQ 459 (U.S. S.Ct. 1966).

The relevant inquiry is whether the prior art suggests the invention and whether the prior art would have provided one of ordinary skill in the art with a reasonable expectation of success. *In re O'Farrell*, 7 USPQ 2d 1673 (Fed. Cir. 1988). Both the suggestion and the reasonable expectation of success *must be founded in the prior art* and not in the Applicant's disclosure (emphasis added) *In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991).

Thus, for the cited combination of references to render the present claims legally obvious under 35 U. S. C. § 103, the relevant issues to be considered are:

- whether Dekany discloses or teaches formation of ions of carbohydrate scaffold;
- whether Neubert discloses or teaches formation of ions of carbohydrate scaffold;
- what was the level of ordinary skill in the art at the time the invention was made;
- determining the differences between the prior art and the claimed invention; and
- whether the differences between the prior art and the claimed invention are such that the subject matter *as a whole* would have been obvious to one of ordinary skill in the art at the time the invention was made.

2.2.1 DEKANY DOES NOT OBIVATE COMPOUNDS OF FORMULA I IN WHICH W IS PRESENT.

In analyzing these issues, Applicants note that Dekany discloses a lipidic moiety containing sugar compound. The Action states that Structure 2 of Dekany meets the limitations of instant Formula I for W being absent.

Applicants respectfully note, however, that the claimed invention does not allow for W being absent. Therefore, it is clear that the compounds of the present invention are distinguished from the prior art based upon this sole fact alone.

2.2.2 DEKANY DOES NOT TEACH COMPOUNDS OF FORMULA I IN WHICH THE SUGAR MOIETY IS SUBSTITUTED.

Furthermore, (and as noted by the Examiner) *Dekany does not teach compounds wherein the sugar moiety is substituted with alkyl or heteroalkyl spacers carrying functional groups that can carry a charge.*

2.2.3 DEKANY TEACHES AWAY FROM THE CLAIMED INVENTION.

Applicants also respectfully note that Dekany, in fact, teaches away from the present invention because it does not contemplate or disclose any compounds in which an ionic complex is formed. Moreover, Dekany only provides support for R groups in the sugar moiety to be selected exclusively from hydroxyl (OH) or O-acetyl (OAc) groups. In contrast, claim 1 of the present invention requires O-alkyl groups and related spacer groups to be attached to -OH or -OAc groups in the compounds discussed in Dekany.

2.2.4 DEKANY AND NEUBERT DO NOT OBTAIN THE CLAIMED INVENTION.

While Applicants note that Neubert discloses that the lipophilicity of drugs can be increased by ion pair formation with lipophilic counterions, the thrust of this reference is based on the premise that ion pairing is shown to effectively increase the lipophilicity and transport of polar drugs across lipid membranes. Furthermore, Neubert discloses simple compounds that form only singly charged compounds (Neubert at p. 745, Table II).

2.2.5 THE CLAIMED INVENTION IS PATENTABLE OVER THE CITED ART.

The present invention is based on the design and use of non-covalently linked compounds such as lipoamino acids and lipoamino saccharides for drug delivery. This work

exploited the active transport mechanisms present in the gastrointestinal mucosa which resulted in a surprising and unexpected discovery that use of such compounds improves the bioavailability of poorly absorbed drugs and peptides so that they can be absorbed by specialized intestinal transporters (see *e.g.*, Specification at page 4; last two paragraphs and Figure 1 and Figure 2). Furthermore, the compounds of the present invention are complex molecules and provide ***polyvalent*** compounds with counterions.

It is submitted that the present invention is distinguished from the prior art firstly because of the nature of the compound and secondly the mechanism of action of the drug in the gastrointestinal mucosa compared to across lipid membranes. Therefore, the present invention provides a method of delivery of the ionic complex compounds which is able to target the active transport mechanism.

Dekany and Neubert (either alone or in combination) do not disclose the complex ionic carbohydrate compounds as claimed in the present invention. Furthermore, the compounds and mechanism considered in Neubert relate to ionizable drugs across biological membranes. In contrast, the claimed invention provides non-covalently linked compounds for drug delivery (including, for example, lipoamino acids and lipoamino saccharides). Moreover, in sharp contrast to the cited art, the present invention provides polyvalent compounds that are active in the gastrointestinal mucosa—a surprising and unexpected property that facilitates their use in improving the bioavailability of drugs and peptides, such that previously poorly-absorbed compounds may be absorbed by specialized intestinal transporters facilitated by the instantly-claimed compounds and derivatives thereof.

Therefore we respectfully submit the differences as discussed above are such that the subject matter as a whole would not have been obvious to one of ordinary skill in the art at the time the invention was made.

2.3 APPLICANTS REQUEST REJOINDER OF THE GROUP II INVENTION UPON ALLOWANCE OF THE GROUP I INVENTION

In the Restriction Requirement dated December 29, 2004, the Examiner determined that the originally-filed claims were drawn to four distinct inventions, set forth as:

- Group I: Claims 1-17 and 19, said to be drawn to compounds represented by formula I, and compositions comprising the same, classified in class 536, subclass 18.7;
- Group II: Claims 18-20, said to be drawn to a method of preparation of compounds of formula I, classified 536, subclass 124;
- Group III: Claims 21-22, said to be drawn to a method of delivery of therapeutically useful molecules in the form of a compound of formula I, classified in class 514, subclass 54; and
- Group IV: Claims 23, said to be drawn to a method of treating and preventing a pathological condition, classified in class 514, subclass 8.

In response to the requirement for restriction, Applicants elected, without traverse, to prosecute the subject matter encompassed by claims 1-17 and 19, *i.e.*, the Group I invention.

Applicants now note for the record that under the current Statutes, and consistent with the C. F. R., the M. P. E. P, and Technology Center 1600 restriction training materials, if the compositions of the Group I restriction are elected for prosecution, then the subject matter of the Group II invention (directed to processes *for making* the compositions of the Group I invention) and that of the Group III and Group IV inventions (each directed to processes *for using* the compositions of Group I), are subject to rejoinder upon the allowance of the corresponding composition claims. As such, Applicants state their affirmative intention to seek rejoinder of the

“process for using” and “process for making” claims upon allowance of claims directed to the products claimed in the Group I invention. Referring to the pertinent part of M. P. E. P. § 821.04(b):

“Where claims directed to a product and to a process of making and/or using the product are presented in the same application, applicant may be called upon under 35 U. S. C. § 121 to elect claims to either the product or a process....(T)he claims to the non-elected inventions will be withdrawn from further consideration under 37 C. F. R. § 1.142....(H)owever, *if applicant elects a claim(s) directed to a product which is subsequently found allowable, withdrawn process claims which depend from or otherwise require all the limitations of an allowable product claim will be considered for rejoinder.* All claims directed to a non-elected process invention must depend from or otherwise require all the limitations of an allowable product claim for that process invention to be rejoined. Upon rejoinder of claims directed to a previously non-elected process invention, the restriction requirement between the elected product and rejoined process(es) will be withdrawn.” (emphasis added).

Thus, by constructive election of the products of the Group I invention for initial prosecution on the merits, Applicants affirmatively state their intention of requesting proper rejoinder of claims directed to processes of making and processes for using such compositions (*i.e.*, the subject matter of the Group II and Group III/IV inventions, respectively), upon allowance of the subject matter of the Group I invention.

Applicants understand that rejoinder of such process claims are proper only if the scope of the product and process claims are coextensive. To that end, Applicants reserve the right to amend the withdrawn claims to reflect coextensive scope with the product claims once such product claims are indicated as allowable.

2.4 PROVISIONAL REQUEST FOR EXAMINER INTERVIEW AFTER FINAL

Applicants hereby state their provisional request for an interview with Examiner Krishnan *before the issuance of an Advisory Action* to specifically address any particular issues

that may remain after consideration of the present paper and entry of the foregoing amendment. Mindful of the timeframe in which the Office is required to reply to Applicants' instant Communication, Applicants' undersigned representative would appreciate the scheduling of such a conference at the Examiner's earliest convenience to finalize amendment and rejoinder of the withdrawn process claims, and allowance of the present application.

2.5 CONCLUSION

It is respectfully submitted that all claims are fully enabled by the Specification, and that all claims are definite and free of the prior art. Applicants believe that all of the concerns of the Examiner have been resolved, and earnestly solicit concurrence by the Examiner and the issuance of a Notice of Allowance in the case with all due speed.

Applicants note for the record their explicit right to re-file claims to one or more aspects of the invention as originally claimed in one or more continuing application(s) retaining the priority claim of the present application.

Should the Examiner have any questions, a telephone call to the undersigned Applicants' representative would be appreciated and in particular in advance of any subsequent action on the merits.



Respectfully submitted,

A handwritten signature in black ink, appearing to read "Mark D. Moore".

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A handwritten signature in black ink, appearing to read "Mark D. Moore".

Mark D. Moore, Ph.D.